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HIV Education Prison Project

HEPP NEWS

HIV EDUCATION PRISON PROJECT

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ABOUT HEPP

HEPP News, a forum for correctional problem solving, targets correctional administrators and HIV/AIDS care providers including physicians, nurses, outreach workers, and case managers. Published monthly and distributed by fax, HEPP News provides up-to-the-moment information on HIV treatment, efficient approaches to administering HIV treatment in the correctional environment, national and international news related to HIV in prisons and jails, and changes in correctional care that impact HIV treatment. Continuing Medical Education credits are provided by the Brown University Office of Continuing Medical Education to physicians who accurately respond to the questions on the last page of the newsletter.

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Screening and Prevention of Tuberculosis in Correctional Facilities

Elsa Villarino, M.D.
Chief, Therapeutic and Diagnostic Studies Unit, Research and Evaluation Branch, Division of Tuberculosis Elimination, Centers for Disease Control and Prevention

In 1998, 3.6% (5,874/100,000) of all active M. tuberculosis (TB) cases reported in the United States were residents of correctional facilities - a TB case rate that is 50 times that of non-incarcerated individuals (1). This high proportion of cases is due to a combination of factors, including the high prevalence of TB infection in the incarcerated population, aggressive case finding among a high-risk group that often has limited access to other health care services, and the ready transmission of TB in these congregate living environments.

3.6% of all active M. tuberculosis cases (TB) reported in the United States were residents of correctional facilities - a TB case rate 50 times that of non-incarcerated individuals.

The factor that most increases the probability that TB infection will progress to active disease is immune deficiency, such as that caused by co-infection with HIV. At year-end 1996, 21,799 (2.3%) of all state and federal prison inmates were known to be infected with HIV (2). The overall rate of confirmed cases of AIDS among the nation's prison population (0.54%) was six times the rate in the U.S. population (0.09%) Thus, one reason residents of correctional facilities have a high risk for TB disease is that a disproportionately high number of them have HIV infection.

The Advisory Council for the Elimination of Tuberculosis (ACET) has recently published a document that advocates developing, implementing, and focusing strategies for TB control among segments of the population identified as having a high TB risk. (3). One strategy that will be reviewed in this article is maintaining aggressive policies for screening the inmates for TB infection, and initiating and completing therapy regimens for latent M. tuberculosis infection (MTB infection) when indicated. Updated guidelines highlighting new regimens and clinical practices for persons with MTB infection are scheduled for release this spring in *MMWR* and the *American Journal of Respiratory Critical Care in Medicine* (4)[1]. This article discusses current guidelines for treating and preventing TB in corrections[2].

Initial Tuberculosis Screening

The following procedures should be used for the initial screening of inmates, depending on their length of stay in the facility and the type of facility (5, 6). According to the Essential Standard P-32 of the National Commission on Correctional Health Care Prison Standards, symptom screening should be done during intake for all new inmates, regardless of anticipated length of sentence ("Standards" available at www.ncchc.org). Any inmate with symptoms suggestive of TB (chronic productive cough, fever, and/or weight loss) should be immediately placed in a negative pressure respiratory isolation room (TB isolation room) and promptly evaluated for TB disease. In addition, tuberculin skin test (TST) screening of all inmates without a documented positive Mantoux skin test result should be mandatory, although this may not be feasible for short-term inmates. Persons with a positive skin test reaction should receive a chest radiograph, a thorough medical evaluation, and consideration for therapy for latent TB infection once active TB is ruled out. Inmates known to have HIV infection should have a chest radiograph as part of the initial screening, regardless of their TST status.

To prevent transmission in some large jails, TB control officials should consider using on-site chest radiography in addition to skin testing to screen all inmates for TB disease at entry into the facility[3]. Such screening is particularly important for large jails where a combination of risk factors (i.e., an incarcerated population with a very high incidence of TB infection and disease, a high prevalence of HIV infection and drug injection, and a rapid turnover of inmates that make TST-based screening inefficient) are present. Jail officials should consult the local TB control officer for assistance in assessing the need and cost-effectiveness of such screening.

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WHAT'S INSIDE

Screening of TB...

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Follow-up Screening

Long-term inmates who have a negative skin test reaction at intake should be skin tested annually to detect skin test conversions. Persons with a documented positive TST result who have not previously received a course of therapy for MTB infection and who do not qualify for MTB prophylaxis should be screened each year for symptoms of TB disease (see qualifications below). Annual chest radiographs are not necessary for the routine follow-up of infected persons, providing a qualified health provider interviews the patient for symptoms of TB disease.

Diagnosis of Latent Mycobacterium Tuberculosis Infection

A positive skin test reaction in a person without symptoms or signs suggestive of TB disease is considered indicative of latent MTB infection. Whenever latent TB infection is suspected, an evaluation to rule out active TB and assess the need for treatment of latent TB infection should be conducted. This evaluation consists of a medical history, physical examination, chest radiography, and, when indicated, bacteriologic studies. HIV testing is also recommended. Any inmate who has symptoms suggestive of TB should be immediately placed in a TB isolation room and promptly evaluated for TB disease. Inmates should not be returned to the general prison housing, until infectious TB disease has been ruled out by qualified medical personnel (See Isolation Guidelines, HEPP News, March 1999).

Correctional facility inmates who have a positive skin test and no symptoms or signs of active TB who are candidates for therapy include:

TST>5mm

- Persons known to have or suspected of having HIV infection, including persons who inject drugs and whose HIV status is unknown
- Close contact of a person with infectious TB
- Persons who have chest radiograph findings suggestive of previous TB and who have received inadequate or no treatment

TST>10mm

- Persons who inject drugs and are known to be HIV negative
- Persons with certain medical conditions (diabetes mellitus, silicosis, low body weight, etc.) that might increase risk of TB disease

Converter

- Persons whose TST reaction converted from negative to positive within the past 2 years (=10mm increase if younger than 35; =15mm increase if older than 35.) (6)

Treatment for MTB Infection

The new guidelines simplify treatment by setting the same duration of dosing regardless of whether patients are co-infected with HIV, by increasing the options for using intermittent (i.e., twice weekly) regimens, and by recommending the use of Rifampin-based short-duration (i.e., 2-4 months) drug regimens (7). Implementation of the new MTB infection management recommendations may lessen some of the continuing problems with adherence to MTB infection treatment in correctional settings. The major changes and additions, some important background information, and the potential applicability of the new guidelines for correctional facility-settings are summarized here.

Table 1. TB Medication Daily and Twice-Weekly Dosing

TB Medication (DOTS recommended)	Daily Dose (mg/kg body weight)	Twice-Weekly Dose
Isoniazid	5 (4-6) up to 300mg	15 (13-17)
Rifampin	10 (8-12) up to 600mg	10 (8-12)
Pyrazinamide	25 (20-30) up to 2.0g	50 (40-60)
Streptomycin	15 (12-18) up to 1.0g	15 (12-18)
Ethambutol	15 (15-20)	45 (40-50)

Adapted from the World Heath Organizations publication: Treatment of Tuberculosis: Guidelines for National Programs. Second ed. 1997.

Treatment Options (See Table 1)

1.Isoniazid for treatment of MTB infection

For all persons deemed to be candidates for MTB infection therapy, regardless of age, and HIV serostatus, the preferred regimen is INH daily for at least 9 months. ACET based this decision on: (1) a review of the findings from prospective, randomized clinical trials conducted in HIV-negative persons that show that 12 months of INH treatment is more effective than 6 months for the prevention of active TB; (2) the results of subanalysis of some of these trials that showed that maximal beneficial effect of INH was mostly associated with therapy that lasted for at least 9 months, and minimal additional benefit was observed for clinical trial participants who had longer (i.e., 12 months) therapy duration; and (3) HIV status is not a significant factor in the effectiveness of TB prophylactic regimens (8-13). Thus, whenever possible, correctional facilities with long-term stays should opt for using a 9-12 month INH regimen for inmates who are deemed eligible for treatment of MTB infection. This treatment may be administered daily or twice weekly under directly observed therapy (DOT).

2. Rifampin and Pyrazinamide for treatment of MTB infection

The 2-month daily regimen of rifampin and pyrazinamide (PZA) is recommended based on a prospective randomized trial of treatment of MTB infection in HIV-infected persons that showed the 2-month regimen to be similar in safety and efficacy to a 12-month regimen of INH. A similar large-scale clinical trial has not been conducted in HIV negative persons; however, the antituberculosis activity of rifampin and PZA is not expected to differ for those with HIV infection and those without HIV infection. Some experts recommend that the 2-month regimen of daily rifampin and PZA also be given by DOT, which can consist of five observed and two self-administered doses each week.

3. Treatment of INH-Resistant TB Infection

Some alternative options for therapy for MTB infection are recommended for use in special situations. For example, for contacts of patients with Isoniazid-resistant, rifampin-susceptible TB, the recommended regimen is Rifampin and Pyrazinamide given daily for 2 months; however, for patients with intolerance to Pyrazinamide, Rifampin given daily for 4 months is recommended. A 4-month Rifampin regimen is recommended based on the efficacy of a similar regimen in both a prospective randomized trial of tuberculin-positive persons with silicosis and non-randomized trial in persons exposed to persons with Isoniazid-resistant TB.

4. Treatment of MTB Infection in those receiving antiretroviral therapy

Complex pharmacologic interactions occur when rifamycins (Rifampin & Rifabutin) are co-administered with some antiretroviral agents, notably protease inhibitors and non-nucleoside reverse transcriptase inhibitors. These drug-drug interactions may result in either an increase or decrease of the blood levels of both rifamycins and antiretrovirals, leading to adverse effects such as a decrease in antiretroviral activity or drug toxicities. Thus, therapy for active TB or MTB infection with rifamycins in HIV-infected persons should always be done in consultation with a physician experienced in the care of patients with TB and HIV co-infection. Except for Efavirenz, Rifampin use is to be avoided with PIs and NNRTIs (see HEPPigram on page 4).

Clinical and Laboratory Monitoring During Therapy for MTB Infection

Before the start of treatment for MTB infection, all inmates should receive a clinical evaluation. They should also receive follow-up evaluations for questioning about side effects and a brief physical assessment to check for signs of hepatitis at least monthly (if receiving Isoniazid alone or Rifampin alone) and at 2, 4 and 8 weeks (if receiving Rifampin and Pyrazinamide). Inmates should be educated about the side effects associated with treatment of MTB infection and at each visit reminded of the need to stop treatment and promptly report to medical personnel if signs and symptoms of hepatoxicity appear (e.g., anorexia, abdominal pain, nausea, vomiting, change in color of urine and feces, jaundice).

Continued on page 4

Letter from the Editor

Dear Colleagues,

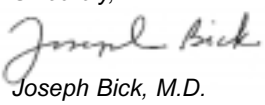
The Ides of March are upon us, and just as in Julius Caesar's time, tuberculosis remains a worldwide scourge. Dramatic decreases in MTB case rates and deaths in the USA this past century belie the worldwide situation. Globally, one person is infected with MTB every second, there are three million MTB related deaths every year, and an estimated one-third of the population is infected with MTB. Rising rates of active MTB among those co-infected with HIV, increasing reports of multiple drug-resistant MTB, and logistical problems associated with the provision of expensive long-term, multi-drug therapy to those least able to afford it, contributed to the World Health Organization's decision to designate MTB as a global emergency in 1995.

Our incarcerated patients often do not readily access healthcare in the free world. We in corrections, therefore, have a unique opportunity and responsibility to make a major public health impact in the area of MTB prevention and treatment. Certainly the Advisory Council for the Elimination of Tuberculosis' goal of worldwide eradication of MTB by 2010 will not be met without the coordinated efforts of all of us working in correctional healthcare!

This month's HEPP News features an article by Elsa Villarino, MD on the Screening and Prevention of TB in Correctional Facilities. Staff testing and strategies for the management of the less cooperative inmate/patient such as those with co-morbid mental illness will be addressed in a future issue. Also this month is a table detailing significant pharmacokinetic interactions between ART and rifamycins; a Heppigram outlining management of MTB in the HIV-infected patient, reports from the 7th Conference on Retroviruses and Opportunistic Infections, and a patient scenario involving an individual co-infected with HIV and MTB. After reviewing this issue, readers should be able to identify candidates for TB screening and treatment, know which TB and HIV medications to recommend and how to manage TB patients co-infected with HIV, and be familiar with the latest updates concerning TB from the 7th Conference on Retroviruses and Opportunistic Infections.

As always, we encourage your comments and suggestions for future HEPP news topics.

Sincerely,



Joseph Bick, M.D.

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NAME: _____

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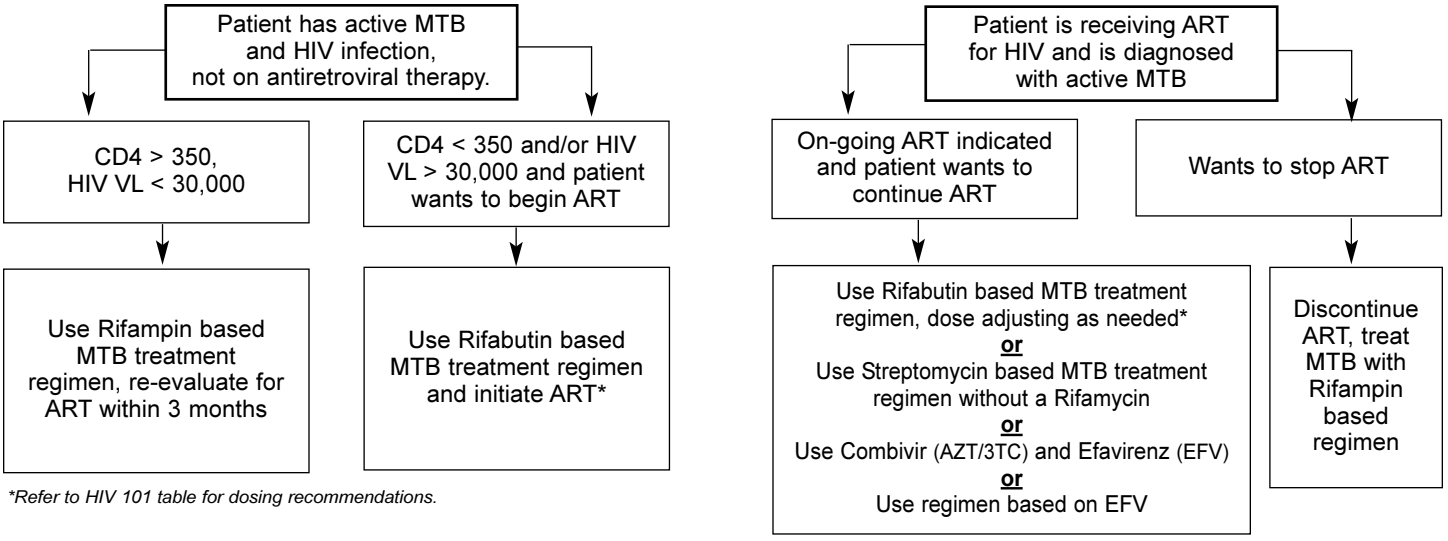
HEPPigram

Recommended Management Strategies for Patients With Both HIV and Active Tuberculosis



**Refer to HIV 101 table for dosing recommendations.*

Screening of TB...

(continued from page 2)

Baseline laboratory testing is not routinely indicated for all persons at the start of treatment for MTB infection, however, based on the relatively high prevalence of chronic liver disease (e.g., Hepatitis B or C, alcoholic hepatitis, or cirrhosis) among the inmate population, baseline hepatic measurements of serum AST (SGOT) or ALT (SGPT) and bilirubin should probably be considered for all persons in this setting. Active hepatitis and end-stage liver disease are relative contraindications to the use of Isoniazid or Pyrazinamide for treatment of MTB infection.

Routine laboratory monitoring during treatment of MTB infection is indicated for persons whose baseline liver function tests are abnormal (>3 times upper level of normal), women who are pregnant, and other persons with a risk of hepatic disease. Laboratory testing may also be indicated for the evaluation of possible adverse effects that occur during the course of treatment (e.g., liver function studies for patients with symptoms compatible with hepatoxicity or a uric acid measurement to evaluate complaints of joint pain). Persons with HIV infection are often treated with multiple drugs in addition to antituberculosis drugs. During the course of treatment for MTB infection all other medications that a person is taking should be reviewed and assessed for potential drug interaction with TB medications. Efforts to manage these potential problems related to drug interactions require the coordinated efforts of clinicians responsible for HIV and TB care (See HEPPigram above).

Conclusion

Control of TB is an essential element in correctional health care. All correctional facilities, even those in which few cases of TB are expected, should have a written plan for the screening and prevention of tuberculosis. State TB officials are available for consultation on the development of this plan. The strategic application of these interventions, however, should be based on the size and type of the facility and the length of stay of the facility's inmates. All TB control personnel and clinicians who treat inmates or staff should be familiar with the special problems that correctional facilities may face arriving at a diagnosis of TB disease or infection. Upon release from correctional facilities, patients should be refered to local health departments in order to keep the disease under control.

When adherence to MTB infection treatment regimens is identified as a problem following the release of the inmates from the correctional facilities, TB control personnel from these institutions, in collaboration with staff from TB control programs at the local level, should seek and develop well-defined procedures for discharge planning, interagency collaborations, and incentives to return for follow-up appointments. The use of new ultra-short course of therapy that may be completed before release may also significantly benefit the control of correctional facility-related TB.

Footnotes

[1]The CDC's National Center for HIV, STD and TB Prevention website (http://www.cdc.gov/nchstp/tb) has the most updated guidelines on TB prevention and treatment, as well as very useful algorithms on TB management. Local TB control officials for each state are also listed at this site.

[2]Abt Associates is currrently working with CDC on a study of the extent of adherence to CDC's guidelines for TB control in a group of large jail systems serving cities with higher than average TB incidence. Later this spring, Abt Associates will be sending a mail survey to these jail systems and the public health departments in these jurisdictions. Following the mail survey they will be conducting site visits to about 20 jurisdictions. CDC will use the study results to review the guidelines and consider strategies for enhancing TB control in jails. Jail systems and health departments that are contacted regarding this study are urged to participate. For further information, contact Dr. Mark Lobato, the CDC Project Officer (404-639-8131) or Dr. Ted Hammett, the Abt Associates Project Director (617-349-2734)

[3]Correctional clinicians might find it useful to employ the mini-chest x-ray cassette-type machines with rolls of 1,000 100x100mm exposures. These avoid excessive radiation exposure to frequent visitors to the jail, save space for the storing of films, and are less expensive than full size films.

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Ask the Expert

Case: *JS is a 44 year-old male who has been incarcerated multiple times since the age of 22. He has a history of IVDU and crack cocaine use, and was diagnosed with HIV in 1988 and HCV in 1996. He refused antiretrovirals until May 1998, when he enrolled in ACTG 388 (AZT, 3TC, and efavirenz). At therapy initiation, CD4 was 22 and CD4% 1.8. The patient did well until July 1998 when AZT was discontinued because of anemia and replaced with d4T. Four weeks later the patient became febrile (105.1 F), tachycardic (130), tachypnic (28), but blood pressure was normal (110/70). The patient also complained of non-productive cough for two months and weight loss. At this time the CD4 was 95 and CD4% 7.3, HIV-1 RNA 130,000 copies/mL.*

Expert Response: Dr. Joseph Bick, M.D. *California Department of Corrections, California Medical Facility, Vacaville*

For those of us practicing in congregate living environments (CLE) such as jails and prisons, JS's diagnosis must be tuberculosis (TB) until proven to be otherwise. Clearly TB is not the most common cause of pneumonia in those who are HIV infected, but because of the devastating public health consequences of a missed or delayed diagnosis, it must be ruled out. An aggressive approach is all the more important in those systems that cluster immunodeficient inmates. In designated HIV CLEs, progression to active TB can occur within four to six weeks after infection and quickly result in an epidemic.

In designated HIV CLEs, progression to active TB can occur within four to six weeks after infection and quickly result in an epidemic.

Faced with JS's presentation, then, the decision must be to place the patient in a negative pressure respiratory isolation room and treat as a TB suspect case. This entails initiating empirical four drug antitubercular therapy (unless major contraindications exist) inducing three sputums for AFB stain and culture, and reporting the patient to the public health department as a TB suspect case.

S. pneumonia, H. influenza, and other bacteria remain the most common causes of pneumonia in those who are HIV infected. Notably, over 80% of S. pneumonia clinical isolates are contained in the current vaccine and are therefore potentially preventable. If the patient's CD4 count is <200, pneumocystis becomes a common cause of pneumonia. Although there is considerable overlap in the presentation of pneumonia due to various organisms, there are some clues to help with the diagnosis. If the PaO2 is <75, the LDH >400, the infiltrates have an interstitial pattern, and the patient has dyspnea on exertion the diagnosis is more likely to be PCP than TB. If weight loss is a prominent feature, the diagnosis is more likely to be TB. However, none of the features is specific enough to enable one to eliminate the possibility of TB.

The presentation of TB can vary depending upon the immune status of the patient. In those with CD4 counts >400, TB is usually a reactivation disease and classically presents with upper lobe disease with or without cavitation. In this setting, extrapulmonary disease is uncommon. In those with lower CD4 counts, 30-50% of cases are primary progressive (active disease develops shortly after infection) rather than reactivation. 25-35% of these patients will have extrapulmonary disease, often in the lymph nodes or bone marrow. Blood cultures are positive 25-50% of the time. The most common chest x-ray abnormality is mediastinal or hilar adenopathy. A diffuse reticulonodular pattern is common. Induced sputum smears are positive in 40-50% of cases of pulmonary TB. Specimens obtained by bronchioalveolar lavage stain positive 50-60% of the time, and cultures are positive in 80-90% of cases.

If a cavity is present on chest x-ray, tuberculosis is the most likely cause. Other organisms that commonly cause cavitary lesions include cryptococcus, coccidioidomycoses, and histoplasmosis. Cryptococcus can present with a reticulonodular pattern, or nodules that may cavitate. For those who have traveled to the southwest, coccidioidomycoses often presents with a reticulonodular pattern and can cause thin walled cavities. For those who have been along the Mississippi valley or in Central/South America, histoplasmosis can present with one to two millimeter nodules that can cavitate. Less common causes of cavities include staphylococcus, pseudomonas, rhodococcus, blastomycoses, and non-tuberculous mycobacteria.

Silver and AFB stains of sputum were negative, and a sputum gram stain showed gram-positive rods. Chest x-ray showed multiple 1-3mm radiopaque lesions on both lung fields. Bronchial lavage was negative for fungus, PCP, AFB stain and malignancy. Previous chest x-ray on June 1998 was normal. Patient was initially treated empirically with Bactrim 5 mg/kg I.V. Q 6 h. A DNA probe was positive for MTB complex. A lung wedge biopsy was negative for malignancy, fungus, and for AFB. Patient was placed in respiratory isolation and treated with INH, Rifabutin, Ethambutol, and Pyrazinamide in addition to the above antiretrovirals, with a diagnosis of miliary Tuberculosis.

In JS's case, a gene probe from one of his respiratory specimens was positive for TB. We should all ensure that the labs which process our mycobacterial specimens do in fact utilize a bactec system and gene probe technology so that positive diagnoses can be made promptly. JS was placed on antitubercular therapy, and, I assume, was released from isolation after 1) he was clinically improved, 2) he had received two weeks of directly observed antitubercular therapy (DOT), and 3) he had three consecutive negative sputum smears for AFB. His TB regimen was selected taking into account potential pharmacokinetic interactions with his ART.

We should all ensure that the labs which process our mycobacterial specimens do in fact utilize a bactec system and gene probe technology so that positive diagnoses can be made promptly.

The patient did well until February 1999 when he developed mild confusion, ataxia and memory loss.

The differential diagnosis at that time was broad, and included drug intoxication, hepatic encephalopathy from his known Hepatitis C, electrolyte abnormalities, endocarditis from his IVDU with CNS

Continued on page 6

Conference News

Tuberculosis and Opportunistic Infection Highlights from the 7th Conference on Retroviruses and Opportunistic Infections

The 7th Conference on Retroviruses and Opportunistic Infections was held January 30 through February 2, 2000, in San Francisco, CA. The following is a synopsis of the abstracts that were relevant to tuberculosis. Next month's issue of HEPP News will review the abstracts related to HIV resistance from the Retrovirus conference.

Abstract 246
This Swiss cohort study evaluated the safety of stopping or withholding primary prophylaxis for disseminated Mycobacterium avium (dMAC) in those whose CD4 count had risen while on ART from <50 to >100. In 253 patients followed for 364 patient-years, no cases of dMAC developed.

Abstract 247
CPCRA study 048 evaluated the benefit of weekly dMAC prophylaxis with azithromycin vs. placebo in those with CD4 previously <50 but now >100 while on ART. 520 patients were followed for a median of 12 months. There were no differences in the percent of individuals who developed dMAC, progression of HIV disease, bacterial pneumonia, or death in the treatment vs. placebo groups.

Abstract 255
This Italian observational study evaluated the risk of HIV infected patients developing active MTB based upon their receipt of ART. Those on no ART had a markedly increased risk as compared to those on ART. Those on at least three agents had one half the risk of those on two agents.

Abstract 258
This abstract from Florida described paradoxical reactions in HIV-infected patients under treatment for MTB who were started on ART. Six patients developed new or worsening CNS lesions after the initiation of ART that did not respond to empiric anti-toxoplasma therapy. Symptoms included headache, weakness, mental status changes, new seizures nausea and emesis. Symptoms began a median of 18 days (10-59) after initiation of ART. All patients required corticosteroids. (See this month's expert case for a discussion of immune reconsitution syndrome).

Abstract 243
In ACTG 88, PCP prophylaxis was withdrawn from two groups: 144 patients with a past history of CD4<100 but now >200 while on ART and 125 patients with a past history of PCP who now had >200 CD4 while on ART. During a follow-up of 46 weeks, no patients in either group developed PCP.

Abstract 230
In this Spanish study, 302 patients with HIV, a past CD4<100, and positive toxoplasma serology currently on ART with CD4 >200 and VL<5000 for at least three months were randomized to either continue or stop toxoplasma prophylaxis. After a 10-month follow-up, there were no cases of toxoplasma encephalitis or death in either group.

Abstract 231
This Roche study evaluated an oral ganciclovir prodrug valganciclovir vs. intravenous ganciclovir in the induction and maintenance therapy of 160 patients with newly diagnosed CMV retinitis. Both regimens yielded similar results in terms of response to therapy and time to progression.

Abstract 250
This intriguing small study (six patients) from UCSF looked at discontinuing cryptococcal meningitis maintenance therapy in HIV infected patients who were asymptomatic for at least four months, had received 12 months of fluconazole, had CD4 >150, and were receiving ART for at least four months. During eight weeks of follow-up, none of the patients became symptomatic or had increases in their serum or CSF cryptococcal antigen titres.

Ask the Expert...

(continued from page 5)

emboli, PML, CNS infectious etiologies such as neurosyphilis, cryptococcus, toxoplasmosis, and a variety of viral encephalitides. If the results of serum glucose, electrolytes, ammonia and CBC did not readily explain his condition, the next step would be to proceed to a brain scan followed by a lumbar puncture.

A CT scan of the brain showed multiple supratentorial hyperdense lesions. MRI of the brain showed multiple enhancing lesions in the central hemispheres.

In JS's case, a brain scan revealed multiple enhancing lesions, which in the setting of HIV disease is most likely due to toxoplasmosis or malignancy (i.e. lymphoma). I will assume that JS had been receiving all of his TB therapy by DOT, his isolate was found to be pansusceptible and had adhered perfectly. If that were not the case, one would also need to worry about CNS tuberculomas as the etiology of his current presentation.

In HIV infected patients with CD4 <200, multiple ring enhancing lesions on brain scan, and a positive serum toxoplasma IgG, the usual practice is to initiate empirical anti-toxoplasma therapy. If there is a lack of response at two weeks, one should consider brain biopsy to rule out other etiologies. In those with less classic brain scan presentations and/or negative toxoplasma IgG, one might consider earlier biopsy. In JS's case, his ART had resulted in a dramatic improvement in his immunologic status with an increase in his CD4 to 580.

On April 1999 a brain biopsy showed tuberculosis encephalitis.

Since the widespread use of highly active ART, numerous syndromes have been described which have been attributed to the host's improved ability to mount an effective immune response to various pathogens. Even in the setting of effective therapy against various opportunistic infections, ART induced immunologic recovery has led to apparent clinical deterioration. Mycobacterium avium has worsened with mesenteric and thoracic adenopathy, CMV retinitis has presented or worsened, chronic Hepatitis B has flared, and TB has worsened with the recurrence of fevers and lymphadenopathy.

Certainly, clinicians must always be on the lookout for a new opportunistic infection (OI) or non-adherence to OI therapy as the cause of such syndromes. However, in the setting of newly initiated ART with virologic and CD4 responses, one must consider the possibility that the patient is experiencing an IRS and not treatment failure.

Save the Dates

Clinical Updates in Correctional Health Care: A Multi Disciplinary Educational Conference
March 19-21, 2000
New Orleans, Louisiana
Call: NCCHC 773.880.1460
Fax: 773.880.2424
Visit: www.ncchc.org

HIV Pathogenesis, Antiretrovirals, and Other Selected Issues in HIV Disease Management
March 22, New York, NY
April 19, Chicago, IL
Aptil 25, San Francisco, CA
May date TBA, Dallas, TX and Washington, DC
Call: 415.56.6725
Fax: 415.56.6740
E-mail: cme@iasusa.org
Visit: www.iasusa.org
Sponsor: International AIDS Society

National Conference on Pharmaceutical Care to Underserved Populations
April 3-4, 2000
Chapel Hill, NC
Call: 919.966.8138
Email: steve_moore@unc.edu
Sponsors: School of Pharmacy and Cecil Sheps Center for Health Services Research, UNC at Chapel Hill, HRSA, NC Assn of Pharmacists
CME available

10th International Symposium on Viral Hepatitis and Liver Disease
April 9-13, 2000
Marriott Marquis, Atlanta Hilton Towers & Hyatt Regency Hotel
Atlanta, GA
Call: Harold Margolis 404.639.2339
Visit: www.HEP2000.com

HIV Prevention with Incarcerated Persons
A Public Health Training Network Satellite Broadcast
April 27, 2000 1:00-3:00 PM EST
Call: 800.458.5231 or TTY 800.243.7012
Visit: www.cdcnpin.org/broadcast
Sponsor: CDC's National Prevention Information Network

10th Annual Clinical Care Options for HIV Symposium
May 4-5, 2000
Scottsdale, AZ
Call: 888.391.3996
Fax: 508.528.7880
Email: registration@mail.medscape.com
Visit: http://hiv.medscape.com/symposium2000
Sponsors: N.W. Univ. Medical School Comprehensive AIDS Center

Drug Use, HIV and Hepatitis: Bringing it All Together
May 7-10, 2000
Baltimore, MD
Call: 877.565.3693
Fax: 301.565.3710
Visit: www.chhatt.net/conference.html
Sponsors: CSAT of SAMHSA, NIDA of NIH, and the CDC.

News Flashes

HAART May Allow Discontinuation of CMV Prophylaxis
Anti-CMV maintenance therapy likely can be safely stopped in some patients on HAART with Cytomegalovirus (CMV) retinitis if CD4+ cell counts are stable or increasing and have been higher than 0.10x109/L for at least 3 months. Immune recovery in patients receiving HAART has been effective in controlling opportunistic infections, but it may also result in intraocular inflammation, which can have adverse effects on the eye. Scott Whitcup, MD, discusses the prevalence of uveitis among 28 patients who have demonstrated a similar clinical course in the February 2 issue of JAMA, (Whitcup, C. JAMA 2/2/2000;283: 653-257.)

FDA Approves Once Daily Dosing for Didanosine
Once-daily dosing is approved for didanosine (200mg tablets), meaning two 200mg tablets once a day. This new dosing exposes patients to 50% less antacid buffer per daily does. The 200mg tablet should not be used for BID dosing, since two tablets are required for adequate buffering. For more information, go to http://www.fda.gov/cder/approval/

GAO Releases Study on Women in Prison
The nation's female inmate population in state and federal prisons in the 1990s doubled, growing faster than the male population, according to a study released January 31 by the General Accounting Office. The study, commissioned by Del. Eleanor Holmes Norton (D-D.C.), also found that the majority of women in prison are incarcerated for nonviolent crimes, are mothers and are incarcerated at great distances from their children, and that women in prison are more likely to suffer from HIV infection and mental illness than men are. The GAO looked specifically at the federal Bureau of Prisons, the California Department of Corrections and the Texas Department of Criminal Justice-the nation's three largest prison systems. Female incarceration for violent crimes in state prisons has decreased from 49 percent in 1979 to 28 percent in 1997, and for property crimes from 37 percent to 27 percent in that period. These findings suggest that women are being incarcerated for drug crimes committed often to feed drug habits and for less serious property crimes than men. The full report is available at http://www.gao.gov/audit.htm.

FDA Public Health Advisory: St. John's Wort, Indinavir and other drugs
The Food and Drug Administration (FDA) issued a Public Health Advisory February 10, 2000 alerting health providers to the risk of drug interactions with St. John's Wort and Indinavir and other drugs. Results from a study conducted by the National Institutes of Health showed a significant drug interaction between St. John's Wort (hypericum perforatum), an herbal product sold as a dietary supplement, and Indinavir, a protease inhibitor used to treat HIV infection. In this study, concomitant administration of St. John's Wort and Indinavir substantially decreased indinavir plasma concentrations, potentially due to induction of the cytochrome P450 metabolic pathway. Consequently, concomitant use of St. John's Wort with PIs or NNRTIs is not recommended because this may result in suboptimal antiretroviral drug concentrations, leading to loss of virologic response and development of resistance or class cross-resistance. For more information, refer to Piscitelli et al. Lancet. 2/12/2000. The health advisory is available at http://hivatis.org/stjohn.html?list

World Tuberculosis Day 2000 Approaches
World TB Day on March 24, 2000 marks a key date for mobilizing political will and encouraging the involvement of civil society in the global efforts to stop TB. The theme, “Forging new Partnerships to Stop TB,” is a call to reach out beyond the TB community and to mobilize new TB constituencies such as international agencies and organizations, women's groups, human rights groups, HIV/AIDS groups, and others to join the global movement to stop TB. For more information go to the WHO TB home page: http://www.who.int/gtb/index.htm

W Variant Outbreak of TB Identified with Population-Based Molecular Epidemiology
Variants of the New York City Strain W of M tuberculosis (TB) were identified in New Jersey using a more sensitive type of epidemiologic study. The population-based cross-sectional study revealed that the TB outbreak in New Jersey included two types of the multi-drug resistant strain W. Groups A (43 patients) shared a unique banding motif not shared by other W family isolates, and group B (25 patients) included strains that did not have that motif. Patients in group A were more likely to be US-born (91%), black (76%), HIV-infected (40%) and residents of urban northeast New Jersey counties. According to Bifani et al, the findings are useful in showing epidemiological outbreak patterns, and they helped to identify a previously unknown outbreak in a specific area. (Bifani PJ, Mathema B, Liu Z, et al. JAMA. 12/29/99; 282(24): 2321).

Coming Next Month . . .

April HEPP News
Main Article: Dr. Rick Altice will discuss the latest news about HIV drug-resistance testing.
HIV 101: Review how to read a gel diagram for common gene mutations.
Ask the Expert: Discuss a deep salvage case.
Spotlight: Highlight the Florida DOC's genotyping plan.

HIV 101

Pharmacokinetic Interactions Between Antiretroviral Agents and Rifamycins

ANTIRETROVIRAL AGENT	RIFAMPIN	RIFABUTIN
NRTIs*	No significant interaction	No significant interaction
Nevirapine (NVP)	NVP decreased 37%. Co-administration not recommended.	No data
Delavirdine (DLV)	DLV decreased 96%. Co-administration contraindicated	DLV decreased 80%. Rifabutin increased 100%. Co-administration not recommended.
Efavirenz (EFV)	EFV decreased 25%. No dose change required.	EFV not changed. Rifabutin decreased 35%. Increase Rifabutin to 450mg QD.
Ritonavir (RTV)	RTV decreased 35%. No data available on dose change.	Rifabutin increased 400%. Decrease Rifabutin to 150mg QOD.
Saquinivir (SQV)	SQV decreased 84%. Co-administration contraindicated.	SQV decreased 40%. Co-administration not recommended.
Nelfinavir (NFV)	NFV decreased 82%. Co-administration contraindicated.	NFV decreased 32%. Rifabutin increased 200%. Decrease Rifabutin to 150mg QD and increase IDV to 1000mg TID.
Indinavir (IDV)	IDV decreased 89%. Co-administration contraindicated.	IDV decreased 32%. Rifabutin increased 200%. Decrease Rifabutin to 150mg QD and increase IDV to 1000mg TID.
Amprenavir (AMP)	AMO decreased 82%. Avoid co-administration.	AMP decreased 15%. Rifabutin increased 193%. No change in AMP. Decrease Rifabutin to 150mg QD.

**Nucleoside reverse transciptase inhibitors.*
Modified from Guidelines for the Use of Antiretroviral Agents in HIV Infected Adults and Adolescents, MMWR October 30, 1998 / 47(RR20); 1-51. Available at www.cdc.gov/mmwr

Resources

Updated *Guidelines* available on the Web
The updated *Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents* is now available on the HIV/AIDS Treatment Information Service (ATIS) at www.hivatis.org in both portable document format (PDF) and web format. Single copies can be ordered at 800.448.0440 or e-mail atis@hivatis.org.

TB Websites:

Morbidity and Mortality Weekly Report on Tuberculosis:
October 30, 1998 / 47(RR20);1-51
www.cdc.gov/mmwr

Francis J Curry National Tuberculosis Center
http://www.nationaltbcenter.edu

Post-Exposure Prophylaxis Network
http://epi-center.ucsf/edu/PEP/pepnet.html

NJ Medical School National TB Center
http://www.undnj.edu/ntbc

Brown University TB/HIV Research Lab
http://www.brown.edu/research/TB-HIV_Lab/

World Health Organization Tuberculosis Website
http://www.who.int/gtb/index.htm

CDC's National Center for STD, HIV, and TB Prevention
http://www.cdc.gov/nchstp/od/nchstp.html

Related Websites:

Medscape HIV/AIDS
http://hiv.medscape.com

Johns Hopkins AIDS Service
http://www.hopkins-AIDS.edu

JAMA HIV/AIDS Information Center
http://www.ama-assn.org/special/hiv

International Association of Physicians in AIDS Care (IAPAC)
http://www.iapac.org

7th Conference on Retroviruses and Opportunistic Infections
http://www.retroconference.org/

Doctor's Guide to the Internet: a straightforward guide to internet medical resources
http://www.docguide.com

AEGIS-AIDS Education Global Information System
http://www.aegis.com

Telephone Numbers:

National Clinicians' PEP Hotline:
888.448.4911

National TB Center at the NJ Medical School:
973.972.3270

TB Infoline
800.4TB.DOCS

National HIV Telephone Consultation Services:
800.933.3413

CDC National AIDS Hotline (24 hours):
800.342.AIDS

Self-Assessment Test for Continuing Medical Education Credit

Brown University School of Medicine designates this educational activity for 1 hour in category 1 credit toward the AMA Physician's Recognition Award. To be eligible for CME credit, answer the questions below by circling the letter next to the correct answer to each of the questions. A minimum of 70% of the questions must be answered correctly. This activity is eligible for CME credit through April 30, 2000. The estimated time for completion of this activity is one hour and there is no fee for participation.

1. Which of the following drugs is acceptable for co-administration with Rifampin?
   a) Nelfinavir (NFV)
   b) Delavirdine (DLV)
   c) Saquinavir (SQV)
   d) Efavirenz (EFV)
   e) Indinavir (IDV)

2. Indicate which of the following sentences are true?
   a) All inmates should be screened for TB signs or symptoms at intake.
   b) Inmates known to have HIV infection should have a chest radiograph as part of the initial screening, regardless of their TST status
   c) Placement in a negative pressure respiratory isolation room is necessary for any inmate who presents with symptoms suggestive of TB.
   d) All of the above
   e) None of the above

3. A patient presents with active MTB and HIV infection who is currently not on ART, and has a CD4 of >350 and viral load of <30,000. How do you initiate treatment?
   a) Use rifabutin-based MTB treatment regimen, and initiate ART (making appropriate dosage adjustments).
   b) Use streptomycin-based MTB treatment regimen.
   c) Use rifampin-based MTB treatment regimen, and re-evaluate for ART within 3 months.
   d) Start either Combivir (AZT/3TC) and EFV or any EFV-based regimen.

4. Which of the following statements are true about differential diagnosis of PCP and TB?
   a) If the PaO2 is less than 75, the LDH is greater than 400, the infiltrates have an interstitial pattern, and the patient has dyspnea on exertion, the diagnosis is more likely to be TB than PCP.
   b) If weight loss is a prominent feature, the diagnosis is definitively TB.
   c) Pneumonia and TB present so similarly the only way to distinguish them is through chest radiograph.
   d) a, b
   e) None of the above features are specific enough to enable one to eliminate the possibility of TB.

5. Which condition(s) may contraindicate the use of Isoniazid or Pyrazinamide?
   a) HIV infection
   b) Diabetes mellitus
   c) Low body weight (10% or more below the ideal)
   d) Active Hepatitis
   e) End-Stage Liver Disease

6. Recent studies have suggested that:
   a) It may be safe to discontinue MAC prophylaxis in those receiving ART with CD4 counts >100
   b) Discontinuation of toxoplasma prophylaxis in those receiving ART whose CD4 counts have risen to >200 leads to an increased risk of toxoplasma encephalitis
   c) It may be safe to discontinue PCP prophylaxis in those on ART whose CD4 count has risen to >100
   d) The rate of completion of two months of pyrazinamide plus rifampin for MTB prevention is significantly less than that of nine to twelve months of daily isoniazid

HEPP News Evaluation

5 Excellent 4 Very Good 3 Fair 2 Poor 1 Very Poor

1. Please evaluate the following sections with respect to:

	educational value	clarity
Main Article	5 4 3 2 1	5 4 3 2 1
HEPPigram	5 4 3 2 1	5 4 3 2 1
HIV 101	5 4 3 2 1	5 4 3 2 1
Updates	5 4 3 2 1	5 4 3 2 1
Save the Dates	5 4 3 2 1	5 4 3 2 1

2. Do you feel that HEPP News helps you in your work? Why or why not?

3. What future topics should HEPP News address?

4. How can HEPP News be made more useful to you?

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